Please add new claim 63 as follows:

63. **(New)** A method according to claim 46 wherein the DmGPCR is DmGPCR9 having a sequence with at least 95% sequence identity to SEQ ID NO:22 and wherein the binding partner is a peptide having a sequence with at least 95% sequence identity to SEQ ID NO:157.

REMARKS

Claims 1 to 62 were pending in the present application. Claims 1-45, 47-58, and 60-62 have been removed from consideration as directed to non-elected inventions. Claims 46 and 59 were examined and rejected. Claim 59 has been amended and new claim 63 has been added. Upon entry of the present "Response", claims 46, 59 and 63 will be pending.

Claim 59 has been amended to further clarify the claimed invention. A Sequence Identifier has been added for DmGPCR9 and the term "represented by" has been replaced with "having a sequence of".

New claim 63 has been added. Support for new claim 63 can be found throughout the specification as filed including, *inter alia*, pages 24 which recites ranges of sequence identity of polypeptides.

No new matter has been added via the foregoing amendments.

In view of the foregoing amendments and arguments that follow, Applicants respectfully request that the rejections be reconsidered and withdrawn.

Enablement

Claims 46 and 59 have been rejected under 35 U.S.C. § 112, first paragraph for alleged lack of enablement. Specifically, the Office Action alleges that "the specification, while being enabling for a method for identifying a compound capable of modulating binding between SEQ ID NO:157 and SEQ ID N:22, does not reasonably provide enablement for a method for identifying a compound capable of modulating binding between a DmGPCR and a DmGPCR binding partner, or DmGPCR9 and SEQ ID NO:157" (Office Action, page 3). Applicants respectfully traverse because the specification enables the skilled artisan to practice the full scope of the subject matter defined by the claims without undue experimentation.

Preliminarily, Applicants would like to thank the Examiner for acknowledging that the specification is enabling for "a method for identifying a compound capable of modulating binding between SEQ ID NO:157 and SEQ ID NO:22". As discussed *supra*, Applicants have amended claim 59 to add a Sequence Identifier for DmGPCR9 and have added new claim 63 directed to "a method for identifying a compound capable of modulating binding between a peptide having a sequence with at least 95% sequence identity to SEQ ID NO:157 and a peptide having a sequence with at least 95% sequence identity to SEQ ID NO:22".

The enablement requirement is met if the specification enables the skilled artisan to determine, without undue experimentation, which species encompassed by a generic claim are effective for their intended purpose. *In re Angstadt*, 537 F.2d 498 (C.C.P.A. 1976). A specification need not demonstrate the operativeness of every species encompassed by a generic claim to satisfy the enablement requirement. *Id.* In *Angstadt* the claimed invention involved a method of

catalytically oxidizing hydrocarbons to form hydroperoxides. Noting that catalytic processes are unpredictable, the Court of Customs and Patent Appeals reversed the Board's decision affirming the Examiners' rejection for lack of enablement because one of ordinary skill in the art could determine the effectiveness of a claimed catalyst by following the procedures outlined in the specification. The court explained that:

> [i]f one skilled in this art wished to make and use a transition metal salt other than those disclosed in appellants' 40 runs [examples], he would merely read appellants' specification for direction how to make and use the catalyst complex to oxidize the alkylaromatic hydrocarbons, and could then determine whether hydroperoxides are, in fact, formed...Since appellants have supplied the list of catalysts and have taught how to make and how to use them, we believe that the experimentation required to determine which catalysts will produce hydroperoxides would not be undue and certainly would not 'require ingenuity beyond that to be expected of one of ordinary skill in the art.'

Id. at 503 (citations omitted). The court also explained that § 112, first paragraph does ***not*** require disclosure of test data for every species covered by a claim because such a requirement would necessitate patent applications with thousands of examples and "would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments." *Id.* at 502. The court concluded that the evidence as a whole, including both the inoperative and operative examples, negated the PTO position that persons of ordinary skill in the art, given its unpredictability, would have to engage in undue experimentation to determine which catalysts would work for their intended purpose. *Id.*

Applicants are not required to provide a specification that demonstrates the activity of every species encompassed by the claims, even in unpredictable arts. *Angstadt*, 537 F.2d at 504. Such a

requirement is not only contrary to established precedent, but is also impracticable and unreasonable. *Id.* Applicants are only required to enable the skilled artisan to determine, without undue experimentation, which modified arginine deiminase polypeptides encompassed by the claims are active, which they have done.

As discussed above, the Office Action acknowledges that the specification enables a method for identifying a compound capable of modulating binding between SEQ ID NO:157 and SEQ ID NO:22. If the skilled artisan wished to make and use a method for identifying modulators of binding other than those for modulating binding between SEQ ID NO: 157 and SEQ ID NO:22, he or she need only review the specification and follow the abundant direction provided regarding how to make and use ***any*** method encompassed by the claims. The experimentation required to determine which putative modulators decrease or increase binding would not be undue and would not require ingenuity beyond that expected of one of ordinary skill in the art because assays assessing modulation of binding were well within the expertise of one of ordinary skill in the art at the time of filing. (See, for example, pages 44, 46-50, Example 5 (Interaction Trap/Two Hybrid System to identify DMGPCR-interacting proteins), Example 8 (reciting several assays to identify Modulators of DmGPCR Activity), Example 9 (assays for DmGPCRs matched with Peptide Ligands), and Example 10 (Competition Assay) of the specification as filed recite several examples of assays suitable for use. Example 9 further recites peptide ligands of DmGPCR1 (9 ligands), DmGPCR4 (4 ligands), DmGPCR6 (22 ligands), DmGPCR6aL and 6bL (97 ligands) and DmGPCR9 (1 ligand). Armed with the ligands identified in Table 6 and the respective DmGPCRs, the skilled artisan could readily determine binding modulators of DmGPCRs defined by the present claims by performing

standard binding assays. Indeed, armed with the identity of other DmGPCRs and the ligands identified using, for example, the Interaction Trap/Two Hybrid System of Example 5, the skilled artisan could readily determine binding modulators of other DmGPCRs. The specification coupled with the state of the art at the time of filing thus enable the skilled artisan to make and use the methods encompassed by the claims without undue experimentation.

The Office Action asserts that:

> Insufficient guidance is provided as to which of the myriad of polypeptide species encompassed by the claim will retain the characteristics of a DmGPCR, a DmGPCR9 or a DmGPCR binding partner. Applicants do not disclose any actual or prophetic examples on expected performance of any of the possible muteins of a DmGPCR, a DmGPCR9 or a DmGPCR binding partner . . . It is known in the art that even single amino acid changes of differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. . .
>
> Since the terms DmGPCR, DmGPCR9 or DmGPCR binding partner encompass species homologs, fragments of the full length polypeptide, and allelic variants, and given the art recognized unpredictability of the effects of mutations on protein function, it would require undue experimentation to practice the claimed method.

(Office Action at pages 3 to 4). As previously explained, however, to satisfy the enablement requirement, Applicants need not provide a specification that demonstrates the activity of every species encompassed by the claims, even in unpredictable arts. *Angstadt*, 537 F.2d at 504. Furthermore, the enablement requirement can be fulfilled by the disclosure of specific examples or by the use of broad terminology. *In re Marzocchi*, 439 F.2d 220, 223-224 (C.C.P.A. 1971). Since the disclosure of experimental examples is not required for fulfillment of the enablement requirement, no basis exists for the contention that the instant application contains no experimental examples to satisfy the enablement requirement.

Moreover, in unpredictable arts, to fulfill the enablement requirement, the specification need not provide guidance that transcends the level of knowledge of those skilled in the art. *Angstadt*, 537 F.2d at 504. Rather, Applicants are only required to enable the skilled artisan to determine, without undue experimentation, binding modulators of DmGPCRS. As previously explained, the specification, coupled with the state of the art, meets this standard. Furthermore, routine experimentation, even if difficult, does not constitute undue experimentation. *PPG Indus., Inc. v. Guardian Indus. Corp.*, 75 F.3d 1558, 1564 (Fed. Cir. 1996). No basis therefore exists for the contention that the specification is not enabling because the relevant art may be unpredictable.

Applicants note that the pending claims are directed at identifying binding modulators. The pending claims are ***not*** directed at identifying compounds that do ***not*** modulate binding. Therefore, even assuming *arguendo* that a "myriad of polypeptide species" exists, Applicants point out a binding modulator will be identified in exactly the same manner for each of the polypeptide species. That the structure of a polypeptide may be altered by a single amino acid change is irrelevant to the present inquiry. What is relevant is whether or not a composition modulates binding of this "altered" polypeptide.

Applicants respectfully point out that high throughput binding assays, for example, are widely seen as routine. Indeed, thousands of compounds a day may be screened in such assays against many different receptors by a single lab technician. Such experimentation, although time consuming and repetitive, does not constitute undue experimentation.

Notwithstanding the foregoing, as discussed *supra*, Applicants have amended claim 59 and have added new claim 63. As discussed above, new claim 63 recites methods of identifying

modulators of binding between a polypeptide having at least 95% sequence identity to a DmGPCR having a sequence of SEQ ID NO:22 and a polypeptide having at least 95% sequence identity to a DmGPCR binding partner having a sequence of SEQ ID NO:157.

Applicants have taught how to make and how to use the claimed methods. The experimentation required to identify binding modulators of DmGPCRS is not be undue and certainly would not 'require ingenuity beyond that to be expected of one of ordinary skill in the art.'

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the enablement rejection.

Written Description

Claims 46 and 59 have been rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking adequate written description. Specifically, the Office Action alleges that "the specification and claims do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to SEQ ID NO:22 and SEQ ID NO: 157 . . . Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO: 157 and SEQ ID NO: 22 are insufficient to describe the genus." (Office Action at page 6). Applicants respectfully traverse because the specification describes the claimed subject matter.

"The purpose of the adequate written description requirement is to ensure that the inventor had possession of the claimed subject matter at the time the application was filed. If a person of

ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate written description requirement is met." *In re Alton*, 76 F.3d 1168, 1175, 37 U.S.P.Q.2d 1578, 1584 (Fed. Cir. 1996). A genus may be adequately described through description of a representative number of species that comprise the genus. *Regents of the Univ. of Calif. v. Eli Lilly and Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997); M.P.E.P. § 2163.

The specification provides written description of the subject matter defined by the claims because, *inter alia*, the specification sufficiently describes preferred modifications to polypeptides and further provides assays with which the art-skilled may test such modified polypeptides. For example, the specification describes conservative substitutions to sequences (Tables I-III). As discussed *supra*, the specification is replete with examples of assays, including binding assays, with which the art skilled may assay for binding modulation in accordance with the claimed methods.

The art-skilled would readily acknowledge that the sequences disclosed in the specification are representative of a genus of sequences. Accordingly, the skilled artisan would reasonably believe that Applicants were in possession of the subject matter defined by the present claims at the time of filing. The specification therefore contains an adequate written description of the claimed subject matter, and Applicants respectfully request withdrawal of the rejection.

The first paragraph of section 112 requires Applicants to describe the subject matter ***defined by the claims***. *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575 (Fed. Cir. 1985); *In re Wilder*, 736 F.2d 1516, 1520 (Fed. Cir. 1984). Applicants are ***not*** required to provide a specification that describes anything and everything upon which the claims could ever be construed

to read. If Applicants were held to such a standard, no specification could ever be deemed to meet the written description requirement. As previously discussed, the specification adequately describes ***the subject matter defined by the present claims***, which is all that the law requires. As the subject matter of claims 46 and 59 is described in the specification such that one of skill in the art would readily agree that the inventors had possession of the claimed invention, Applicants respectfully request the reconsideration and withdrawal of the written description rejection.

Notwithstanding the foregoing, Applicants have amended claim 59 and added new claim 63. As discussed above, new claim 63 recites methods of identifying modulators of binding between a polypeptide having at least 95% sequence identity to a DmGPCR having a sequence of SEQ ID NO:22 and a to a DmGPCR binding partner having at least 95% sequence identity with a sequence of SEQ ID NO:157. The species and subgenus defined by amended claim 59 and new claim 63, respectively, is not highly variant—the distinguishing attributes shared by the members of the subgenus is that they share at least 95% sequence identity to SEQ ID NO:157 or to SEQ ID NO:22. Applicants assert that the subject matter of amended claim 59 and new claim 63 is described in the specification such that one of skill in the art would readily agree that the inventors had possession of the claimed invention.

For the foregoing reasons, Applicants respectfully request withdrawal of the written description rejection.

Indefiniteness

Claims 46 and 59 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly

indefinite in the recitation of the terms "DmGPCR", "DmGPCR9", and "represented". Applicants respectfully traverse.

As a preliminary matter, Applicants note that a claim complies with the second paragraph of §112 so long as it is understandable and defines the subject matter which applicant regards as his invention. *In re Kamal*, 158 U.S.P.Q. 320 (C.C.P.A. 1968). Claims 46 and 59 satisfy this standard. There is nothing unclear in their language, and persons skilled in the art would have no difficulty in understanding the meaning of the claim language.

The term "DMGPCR" is well-known to the art-skilled and is defined throughout the specification as filed. For example, page 5, lines 11-12, defines DmGPCR as "Drosophila melanogaster G Protein Coupled Receptor". Additionally as set forth on page 6 of the application as filed, "the term 'DmGPCR' as used herein in singular form is intended to encompass each of the ten amino acid sequences exemplified below, encoded by the respective polynucleotide sequences. Applicants respectfully assert that the instant usage of the term "DmGPCR" would readily be understood by one of ordinary skill in the art as clear and definite.

The term "DmGPCR9" is also described throughout the specification as filed and would also be understood by one of ordinary skill in the art. For example, as set forth on page 67 of the specification, SEQ ID NO: 21 sets forth the nucleotide sequence of DmGPCR9 while SEQ ID NO:22 sets forth the amino acid sequence for the protein encoded by SEQ ID NO:21. One of skill in the art would readily understand the term "DmGPCR9" as clear and definite.

The term "represented" would be readily understood by one of ordinary skill in the art. Notwithstanding the foregoing, solely in an effort to advance the prosecution of the pending claims

to allowance, Applicants have amended claim 59 to further clarify the claim, rendering the rejection as it pertains to the term "represented" moot.

In view of the foregoing, Applicants respectfully request the reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, second paragraph.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned **"Version with markings to show changes made."**

Change of Correspondence Address

As set forth on the attached "Change of Correspondence Address" form SB-122, Applicants respectfully request that all future correspondence related to this application be directed to:

Gwilym J. O. Attwell
COZEN O'CONNOR, P.C.
1900 Market Street
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Telephone: (215) 665-2000
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Conclusion

Applicants believe that the foregoing constitutes a complete and full response to the Office Action of record and the claims are in condition for ready allowance. Accordingly, an early and favorable Action is requested respectfully. If the Examiner feels a telephonic interview would be beneficial, the Examiner is requested to call the undersigned at (215) 665-6904.

Respectfully submitted,

Date: October 29, 2002

Gwilym J. O. Attwell
Registration No. **45,449**

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Enclosure: "Change of Correspondence Address" form SB-122

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please amend claim 59 as follows:

59. **(Amended)** A method according to claim 46 wherein the DmGPCR is DmGPCR9 having a sequence of SEQ ID NO:22 and wherein the binding partner is a peptide [represented by] having a sequence of SEQ ID NO:157.

Please add new claim 63 as follows:

63. **(New)** A method according to claim 46 wherein the DmGPCR is DmGPCR9 having a sequence with at least 95% sequence identity to SEQ ID NO:22 and wherein the binding partner is a peptide having a sequence with at least 95% sequence identity to SEQ ID NO:157.